

Appl. No. 10/076,248  
Reply to Office action of August 2, 2005  
Response dated January 30, 2006

**AMENDMENTS TO THE CLAIMS:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

Claim 1 (Original) A modified synthetic nucleic acid molecule wherein said modification enhances the stability of the nucleic acid molecule comprising:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a pre-mRNA expressed within the cell;
- b) a 3' splice region comprising a branch point, a pyrimidine tract and a 3' splice acceptor site; and
- c) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

Claim 2 (Original) A modified synthetic nucleic acid molecule wherein said modification enhances the stability of the nucleic acid molecule comprising:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a pre-mRNA expressed within the cell;
- b) a 3' splice acceptor site; and
- c) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

Claim 3 (Original) A modified synthetic nucleic acid molecule wherein said modification enhances the stability of the nucleic acid molecule comprising :

- a) one or more target binding domains that target binding of the nucleic acid molecule to a pre-mRNA expressed within the cell;
- b) a 5' splice site; and

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c) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA; wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

**Claim 4 (Original)** The modified synthetic nucleic acid molecule of claim 1 wherein the nucleic acid molecule further comprises a 5' donor site.

**Claim 5 (Original)** The modified synthetic nucleic molecule of claim 1, 2, 3 or 4 further comprising a spacer region that separates the 3' splice region from the target binding domain.

**Claim 6 (Original)** The modified synthetic nucleic acid molecule of claim 1, 2, 3, or 4 further comprising a safety sequence comprising one or more complementary sequences that bind to one or both sides of the 3' splice site.

**Claim 7 (Original)** The modified synthetic nucleic acid molecule of claim 1, 2, 3, or 4 wherein the binding of the nucleic acid molecule to the target pre-mRNA is mediated by complementary, triple helix formation, or protein-nucleic acid interaction.

**Claim 8 (Original)** The modified synthetic nucleic acid molecule of claim 5 wherein the binding of the nucleic acid molecule to the target pre-mRNA is mediated by complementary, triple helix formation, or protein-nucleic acid interaction.

**Claim 9 (Original)** The modified synthetic nucleic acid molecule of claim 6 wherein the binding of the nucleic acid molecule to the target pre-mRNA is mediated by complementary, triple helix formation, or protein-nucleic acid interaction.

**Claim 10 (Original)** The modified synthetic nucleic acid molecule of claim 1, 2, 3 or 4 wherein the nucleotide to be *trans*-spliced to the target pre-mRNA encodes a translatable polypeptide.

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Claim 11 (Original) The modified synthetic nucleic acid molecule of claim 5 wherein the nucleotide to be *trans*-spliced to the target pre-mRNA encodes a translatable polypeptide

Claim 12 (Original) The nucleic acid molecule of claim 6 wherein the nucleotide to be *trans*-spliced to the target pre-mRNA encodes a translatable polypeptide.

Claim 13 (Original) The modified synthetic nucleic acid molecule of claim 1, 2, 3 or 4 wherein the nucleotide sequence to be *trans*-spliced to the target pre-mRNA contains a nonsense mutation.

Claim 14 (Original) The modified synthetic nucleic acid molecule of claim 5 wherein the nucleotide sequence to be *trans*-spliced to the target pre-mRNA contains a nonsense mutation.

Claim 15 (Original) The modified synthetic nucleic acid molecule of claim 6 wherein the nucleotide sequence to be *trans*-spliced to the target pre-mRNA contains a nonsense mutation.

Claim 16 (Original) A modified synthetic nucleic acid molecule wherein said modification enhances the stability of the nucleic acid molecule comprising:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a pre-mRNA expressed within the cell;
- b) a 3' splice region comprising a branch point, a pyrimidine tract and a 3' splice acceptor site; and
- c) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA; wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

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Claim 17 (Original) A modified synthetic nucleic acid molecule wherein said modification enhances the stability of the nucleic acid molecule comprising:

a) one or more target binding domains that target binding of the nucleic acid molecule to a pre-mRNA expressed within the cell;

b) a 3' splice acceptor site; and

c) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA;  
wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

Claim 18 (Original) A modified synthetic nucleic acid molecule wherein said modification enhances the stability of the nucleic acid molecule comprising:

a) one or more target binding domains that target binding of the nucleic acid molecule to a pre-mRNA expressed within the cell;

b) a 5' splice site; and

c) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA;  
wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

Claim 19 (Original) The modified synthetic nucleic acid molecule of claim 16 wherein the nucleic acid molecule further comprises a 5' donor site.

Claim 20 (Original) The modified synthetic nucleic molecule of claim 16, 17, 18 or 19 further comprising a spacer region that separates the 3' splice region from the target binding domain.

Claim 21 (Original) The modified synthetic nucleic acid molecule of claim 16, 17, 18 or 19 further comprising a safety sequence comprising one or more complementary sequences that bind to one or both sides of the 3' splice site.

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Claim 22 (Original) The modified synthetic nucleic acid molecule of claim 16, 17, 18 or 19 wherein the binding of the nucleic acid molecule to the target pre-mRNA is mediated by complementary, triple helix formation, or protein-nucleic acid interaction.

Claim 23 (Original) The modified synthetic nucleic acid molecule of claim 20 wherein the binding of the nucleic acid molecule to the target pre-mRNA is mediated by complementary, triple helix formation, or protein-nucleic acid interaction.

Claim 24 (Original) The modified synthetic nucleic acid molecule of claim 21 wherein the binding of the nucleic acid molecule to the target pre-mRNA is mediated by complementary, triple helix formation, or protein-nucleic acid interaction.

Claim 25 (Original) The modified synthetic nucleic acid molecule of claim 16, 17, 18 or 19 wherein the nucleotide to be *trans*-spliced to the target pre-mRNA encodes a translatable polypeptide.

Claim 26 (Original) The modified synthetic nucleic acid molecule of claim 20 wherein the nucleotide to be *trans*-spliced to the target pre-mRNA encodes a translatable polypeptide.

Claim 27 (Original) The nucleic acid molecule of claim 21 wherein the nucleotide to be *trans*-spliced to the target pre-mRNA encodes a translatable polypeptide.

Claim 28 (Original) The modified synthetic nucleic acid molecule of claim 16, 17, 18 or 19 wherein the nucleotide sequence to be *trans*-spliced to the target pre-mRNA contains a nonsense mutation.

Claim 29 (Original) The modified synthetic nucleic acid molecule of claim 20 wherein the nucleotide sequence to be *trans*-spliced to the target pre-mRNA contains a nonsense mutation.

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Claim 30 (Original) The modified synthetic nucleic acid molecule of claim 21 wherein the nucleotide sequence to be *trans*-spliced to the target pre-mRNA contains a nonsense mutation.

Claim 31 (Previously Presented) The nucleic acid molecule of claim 1, 2, 3, 4, 16, 17, 18, or 19 further comprising a nuclear localization signal.

Claim 32 (Previously Presented) The nucleic acid molecule of claim 1, 2, 3, 4, 16, 17, 18, or 19 wherein said nucleic acid molecule is a circular molecule.

Claim 33 (Previously Presented) The nucleic acid molecule of claim 1, 2, 3, 4, 16, 17, 18, or 19 further comprising an enhancer sequence.

Claim 34 (Previously Presented) A composition comprising a physiological acceptable carrier and a nucleic acid molecule according to claim 1, 2, 3, 4, 16, 17, 18, or 19.

Claim 35 (Cancelled)

Claim 36 (Original) An expression vector comprising an RNA polymerase promoter and a nucleic acid molecule comprising:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a pre-mRNA expressed within the cell;
- b) a 3' splice region comprising a branch point, a pyrimidine tract and a 3' splice acceptor site; and
- c) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA; wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

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Claim 37 (Original) An expression vector comprising an RNA polymerase promoter and a nucleic acid molecule comprising:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a pre-mRNA expressed within the cell;
- b) a 3' splice acceptor site; and
- c) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA; wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

Claim 38 (Original) An expression vector comprising an RNA polymerase promoter and a nucleic acid molecule comprising:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a pre-mRNA expressed within the cell;
- b) a 5' splice site; and
- c) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA; wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

Claim 39 (Original) The expression vector of claim 36 wherein the nucleic acid molecule further comprises a 5' donor site.

Claim 40 (Original) The expression vector of claim 36, 37, 38 or 39 further comprising a spacer region that separates the 3' splice region from the target binding domain.

Claim 41 (Original) The expression vector of claim 36, 37, 38 or 39 further comprising a safety sequence comprising one or more complementary sequences that bind to one or both sides of the 3' splice site.

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Claim 42 (Original) The expression vector of claim 36, 37, 38 or 39 wherein the binding of the nucleic acid molecule to the target pre-mRNA is mediated by complementary, triple helix formation, or protein-nucleic acid interaction.

Claim 43 (Original) The expression vector of claim 40 wherein the binding of the nucleic acid molecule to the target pre-mRNA is mediated by complementary, triple helix formation, or protein-nucleic acid interaction.

Claim 44 (Original) The expression vector of claim 41 wherein the binding of the nucleic acid molecule to the target pre-mRNA is mediated by complementary, triple helix formation, or protein-nucleic acid interaction.

Claim 45 (Original) The expression vector of claim 36, 37, 38 or 39 wherein the nucleotide to be *trans*-spliced to the target pre-mRNA encodes a translatable polypeptide.

Claim 46 (Original) The expression vector of claim 40 wherein the nucleotide to be *trans*-spliced to the target pre-mRNA encodes a translatable polypeptide.

Claim 47 (Original) The expression vector of claim 41 wherein the nucleotide to be *trans*-spliced to the target pre-mRNA encodes a translatable polypeptide.

Claim 48 (Previously Presented) A method for synthesizing the nucleic acid molecule of claim 1, 2, 3, or 4 wherein said nucleic acid molecule is chemically synthesized.

Claim 49 (Previously Presented) A method for synthesizing the nucleic acid molecule of claim 1, 2, 3, or 4 wherein said nucleic acid molecule is synthesized *in vitro*.

Claim 50 (Original) A modified synthetic nucleic acid molecule wherein said modification enhances the stability of the nucleic acid molecule comprising:

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(a) one or more target binding domains that target binding of the nucleic acid molecule to a pre-mRNA expressed within a cell;  
(b) a 5' donor site;  
(c) a 3' splice acceptor site;  
(d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;  
wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

**Claim 51 (Original)** The modified synthetic nucleic acid molecule of claim 50 further comprising a spacer region that separates the 3' splice region from the target binding domain.

**Claim 52 (Original)** The modified synthetic nucleic acid molecule of claim 50 further comprising a safety sequence comprising one or more complementary sequences that bind one or both sides of the 3' splice site.

**Claim 53 (Previously Presented)** The nucleic acid molecule according to claim 1, 2, 3, 4, 16, 17, 18, or 19 associated with a liposome.

**Claim 54 (Previously Presented)** A method of producing a chimeric RNA molecule in a cell comprising contacting the cell with the nucleic acid molecule of claim 1, 2, 3 or 4.

**Claim 55 (Previously Presented)** The method of claim 54 wherein the nucleic acid molecule further comprises a 5' donor site.

**Claim 56 (Previously Presented)** The method of claim 54 wherein the nucleic acid molecule further comprises a spacer region that separates the 3' splice region from the target binding domain.

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Claim 57 (Previously Presented) The method of claim 54 wherein the nucleic acid molecule further comprises a safety sequence comprising one or more complementary sequences that bind to one or both sides of the 3' splice site.

Claim 58 (Previously Presented) The method of claim 54 wherein the binding of the nucleic acid molecule to the target pre-mRNA is mediated by complementary, triple helix formation, or protein-nucleic acid interaction.

Claim 59 (Previously Presented) The method of claim 54 wherein the nucleotide to be *trans*-spliced to the target pre-mRNA encodes a translatable polypeptide.

Claim 60 (Previously Presented) The method of claim 54 wherein the nucleotide sequence to be *trans*-spliced to the target pre-mRNA contains a nonsense mutation.